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Atty. Docket No.: P71641US0

REMARKS

The Final Office Action mailed August 1, 2008, has been received and carefully reviewed. Claims 1-16 and 41-55 are withdrawn. Claims 17-33, 35-40 and 56 are currently undergoing examination. A Request for Continued Examination and Petition for a Three-Month Extension of Time accompanies this response.

Applicant wishes to thank the Examiner for the telephonic interviews of October 16 and October 20, 2008, when the rejection over Wachtel et al. was discussed in detail.

Rejections under 35 U.S.C. §102(b)

The Examiner has maintained the rejection of claims 17-36 under 35 U.S.C. §102(b), as allegedly being anticipated by Wachtel et al, German Patent DE 4037447 ("Wachtel"). According to the Examiner, Wachtel teaches an amino acid composition consisting of histidine, isoleucine, valine, threonine, methionine, leucine, etc., and teaches weight ratios which the examiner calculates to be within the claimed ranges of Applicant's invention. Therefore, according to the Examiner, Wachtel anticipates Applicant's claims. Applicant respectfully traverses this rejection.

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The weight ranges relied upon by the Examiner are calculated based on the deviations identified in Wachtel as the percent deviation of the reported weight percent of the amino acid. As such, the ratio of leucine to valine can be as large as 111.1 to 64.8, or about 1.71:1, which is less than Applicant's claimed ratio of 2:1. The weight ratio of leucine to isoleucine can be as large as 111.1 to 53.6, or about 2.07:1, which is less than Applicant's claimed ratio of than 3:1.

In the Final Rejection, the Examiner asserted that one of skill in the art would interpret the percent deviations presented in column 5, and claim 4, of Wachtel as weight percent deviations, and therefore the reported ranges for the amounts of the various amino acids fall within the scope of Applicant's claimed invention. Applicant submits that one of ordinary skill in the art, when reading Wachtel, would not have understood these percent deviations in this way. Instead, Applicant submits that a person of skill in the art would have understood that the deviations are not weight percent ranges, but the percent deviation of the stated weight percent value of each individual amino acid component. In other words, 5.0

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weight% \pm 20% means a range of 4.0 wt% to 6.0 wt% (20% of 5.0 is 1.0), not a range of -15 wt% to 25 wt%.

Applicant's position is evidenced in the enclosed Declaration of Jan Ruud Hansen under 37 C.F.R §1.132, and which is found as Attachment A to this response ("Hansen Decl."). Mr. Hansen is an expert in the field of statistical data analysis (i.e. the field in which the weight percent deviations of Wachtel are presented), and explains what one of ordinary skill in the art would understand that Wachtel teaches.

As explained by Mr. Hansen, one of ordinary skill in the art would understand that the percentage deviation (\pm %) reported in the table in claim 4 of Wachtel is a percentage deviation of the unit given in the table header, which is weight-percentages. Thus, a (\pm 20%) deviation of 5.0 weight% gives a range of 4.0 to 6.0 weight%. (Hansen Decl. ¶ 9). Similarly, a (\pm 20%) deviation of 5.0 mg gives a range of 4.0 to 6.0 mg. Id. This is the only possible (or reasonable) interpretation of the percentage deviation (\pm %) in the table in Claim 4 of Wachtel.

There are no indications in Wachtel that the deviations should or could be understood as a percentage of the total. (Hansen Decl. ¶9). Wachtel states that "the proportions

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of lysine, isoleucine, leucine, valine and tyrosine can deviate by up to $\pm 10\%$ and for the remaining amino acids by up to $\pm 20\%$ of the mentioned value" (Wachtel (English translation), p. 11). The units for the proportions are in weight% and the units for the deviations are % of the weight% value (see, Wachtel, claim 4).

The table on page 10 mentions a weight% value of 14.5 for the proportion of lysine (Hansen Decl. ¶9). Because 10% of 14.5 equals 1.45, and the unit for the mentioned value is weight%, Wachtel teaches that proportion of lysine can vary in the range 13.05 - 15.95 weight% depending on the individual metabolism situation (Id.). The values presented in Wachtel are relative quantities of amino acids added to a diet, or a recipe (Id.). One of ordinary skill in the art reading Wachtel would understand what the approximate weight% of each ingredient or amino acid should be in proportion to the total amount in the diet. The values in the table are not the result of an experimental determination of a value (Id.).

The amounts of added amino acid component shown in Wachtel are under direct control of the person making the diet. An analogy can be made to a recipe for a cake. One would not expect a recipe for a cake which called for 4 cups of flour $\pm 20\%$

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to mean 4 cups of flour ± 20 cups of flour. The only purported confusion in the case of Wachtel stems from the fact that the units for the amount of each component is weight%, rather than an absolute amount (such as grams, or cups, etc.) (Hansen Decl. ¶9).

Furthermore, if one were to prepare a composition which included a number of ingredients, it would not make sense, to one of ordinary skill in the art, to disclose an amount of 5 wt% $\pm 20\%$ to mean that the amount of compound added to the composition could vary from 0 to 25 weight%, when one could have just as easily stated the range as 0 - 25 weight%, or, in the alternative, stated the range as (12.5 ± 12.5) wt%, and therefore not state a negative range. (Hansen Decl., ¶10).

In view of Applicant's claim 22, the claimed composition contains substantially less lysine than the supplement taught in Wachtel. Claims 23 to 32 are all dependent on claim 22. Applicant submits that claims 22 to 32 cannot be anticipated by Wachtel because all the features of Applicant's claims are not taught by Wachtel.

As stated in Applicant's Response to the previous Office Action, with regard to claim 33, Applicant again points out that the Examiner has miscalculated the weight ratios.

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Thus, the comparison in Table 1 of the Office Action should correctly be as follows:

Amino acid	LNAA of claim 33 (mg in 500 mg total)	Wachtel (mg in 500 mg total)
Tyrosine	100-290	72-88
Tryptophan	25-75	14.4-21.6
Methionine	15-50	19.6-29.4
Isoleucine	15-55	53.6-65.5
Threonine	15-50	38-57
Valine	15-55	64.8-79.2
Leucine	15-200	90.9-111.1
Histidine	10-30	20-30
Lysine	5-200	65.3-79.8

As such, the content of tyrosine and tryptophan is substantially higher in Applicant's supplement defined by claim 33 than taught by Wachtel, and the content of valine in Applicant's supplement is substantially lower. Once again, this means that Wachtel cannot anticipate claim 33.

The Examiner states that percentage deviations less than 0% - as calculated in the way she asserts Wachtel should be understood - would be understood by those of skill in the art to be 0% and would be the lower limit of any such range (Final

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Rejection, p. 4). The Examiner goes on to state this is standard practice in the art. Applicant respectfully disagrees.

The Examiner has not provided any such example in the art which teaches a formula for a composition where the components are expressed in weight%, with percent deviations also in weight%, or its equivalent, that can result in zero or negative values, in the same manner as associated with the Examiner's interpretation of Wachtel. One of ordinary skill would understand that the examples to which the Examiner is referring are generally understood to be due to "rounding errors" introduced when percentages of individual component values are rounded to the next whole percent (Hansen Decl. ¶ 11). In that situation, if one of skill were to add the various component percentages, one could arrive at a sum with a number greater than 100%. This is not the case in Wachtel. The values stated are the proportion of amino acids added in the diet recipe, and there is no teaching regarding the rounding of the percentage values (Id.)

Wachtel states that "If one (or many) amino acids is used in a large quantity, then, it is obvious that one (or many) other amino acids is used in a smaller proportion" (Wachtel (English translation), p. 11). Based on this statement one of

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ordinary skill in the art would appreciate that the total obviously must be 100 weight% (Hansen Decl., ¶11).

In view of the foregoing, including both the arguments made herein and the evidence of the Hansen Declaration, Applicant submits that Wachtel does not teach each and every element of Applicant's claimed invention, and therefore, cannot be anticipated by Wachtel. Accordingly, Applicant respectfully requests withdrawal of this rejection.

Claim Rejections under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 37-40 as being unpatentable under 35 U.S.C. § 103(a), over Wachtel, in view of Ghadimi, and further, in view of Nakaki. According to the Examiner, Wachtel teaches a supplement which anticipates the ranges of all the amino acids except arginine. Ghadami is offered by the Examiner for teaching a LNAA supplement which contains arginine. The Examiner argues that it would have been obvious to one of ordinary skill at the time the invention was made, to add arginine in the amount taught in Ghadimi to the composition of Wachtel because they are both amino acid compositions and, further, because Nakaki teaches that treatment of PKU is started from the time a person is an

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infant, and arginine is a necessary amino acid for growing children. Applicant respectfully traverses this rejection.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

As stated in Applicant's previous amendment, the Examiner's comparison of the supplement in claim 37 to that taught by Wachtel is also based on the same miscalculation as discussed above in connection with the rejection under § 102(b). Thus, the comparison in Table 2 of the Office Action should correctly be as follows:

Amino acid	LNAA of claim 37 (mg per 600 mg total)	Wachtel (mg in 600 mg total)
Tyrosine	100-290	86.4-105.6
Tryptophan	30-90	17.3-25.9
Methionine	25-75	23.5-35.3
Isoleucine	15-45	64.3-78.5
Threonine	15-50	45.6-68.4
Valine	15-50	77.8-95.0
Leucine	40-200	109.1-133.3
Histidine	15-45	24-36
Arginine	15-50	0

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From this Table, it is clear that the content of tryptophan and arginine in Applicant's claimed invention is substantially higher than taught by Wachtel, and that the content of isoleucine and valine recited in Applicant's claims are substantially lower. Nothing in Ghadimi teaches or suggests curing these deficiencies.

Furthermore, one of ordinary skill would have understood that Ghadimi teaches amino acid compositions for intravenous administration directly into the big vessels or into the peripheral veins of a patient (col. 3, lines 63-65). In contrast, Applicant's claimed invention is formulated for enteral, or oral administration. It is clear that one of ordinary skill in the art, when reading Ghadimi, would not have sought to combine the teachings of Wachtel and Ghadimi, and would, in addition, have understood that the compositions of Ghadimi are not suitable for oral or enteral use, as in Applicant's present invention. Furthermore, one of skill would know that the various mixtures disclosed in Ghadimi are not suitable for patients with Phenylketonuria or phenylalanemia, as they all contain the amino acid phenylalanine.

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Nakaki teaches that arginine is known as a necessary nutritional supplement for infants and growing children who cannot synthesize arginine fast enough to support growth requirements (Nakaki at page 1, first paragraph). Contrary to the Examiner's assertion, however, there is no mention of PKU in Nakaki. One of ordinary skill in the art would have understood the main thrust of Nakaki is to teach that oral administration of arginine exerts antihypertensive and antiproliferative effects on vascular smooth muscle, and that the mechanism for this action in the body is poorly understood (page 170, last paragraph). Nowhere in Nakaki is treatment of phenylketonuria, phenylalanemia, or any another amino acid metabolic disorder, taught or suggested.

None of the three references cited by the Examiner teach or suggest that one can treat a patient with an amino acid metabolic disorder, such as phenylketonuria, by administering a diet substantially free of the target amino acid, such as phenylalanine, and which contains a second amino acid which competes with the target amino acid at a gastric transport or uptake site.

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Applicant respectfully submits that one of ordinary skill in the art would not have had any motivation to combine the teachings of Wachtel with that of Ghadimi or Nakaki to arrive at Applicant's claimed invention. Ghadimi does not teach oral or enteral amino acid supplementation for patients with any amino acid metabolism disorders, nor does it teach anything about PKU or phenylalaninemia. Nakaki does not teach anything about PKU or phenylalaninemia either, and merely states that arginine is needed in the diet for growth. Further, none of the references teach the specific ratios of amino acids in a dietary supplement for treatment of patients with amino acid metabolism disorders as claimed by Applicant. Thus, there exists no teaching or suggestion, in any of the cited references, individually, or when combined, to develop Applicant's claimed composition having the specific ratios of amino acids in a dietary supplement, for treatment of patients with amino acid metabolism disorders, as claimed by Applicant.

In view of the foregoing, Applicant submits that the combination of Wachtel, in view of Ghadimi and Nakaki, does not teach or suggest each and every feature of Applicant's claimed invention, and therefore cannot render Applicant's claims *prima*


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facie obvious. Applicant respectfully requests withdrawal of this rejection.

Conclusion

Applicant believes the currently pending claims are now in condition for allowance. If the Examiner has any questions regarding this response, the Examiner is invited to telephone Applicant's counsel at the number provided below.

Respectfully submitted,
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HBJ/WW

CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing ***Applicant's Response to Opposer's First Set of Interrogatories and Requests for Production of Documents and Things*** was served on this 30th day of January, 2009 by first class mail, postage prepaid, addressed to Lauren T. Estrin, Kilpatrick Stockton LLP, 1100 Peachtree Street, Suite 2800, Atlanta, Georgia 30309-4530, Attorney for Opposer.

/Robert S. Pierce/